1459 POSTER

HE4 Levels in Endometrial Cancer Patients − Potential Role as a Tumour Biomarker

L. Zanotti[1], E. Bignotti[1], E. Bandiera[1], S. Calza[2], G. Ruggeri[3], C. Romani[1], A.R. Tassi[1], M. Ragnoli[1], S. Pecorelli[1], A. Ravaggi[1]. *[1]Brescia University, Materno Infantile e Tecn. Biom., Brescia, [2]Brescia University, Scienze Biomediche e Biotecnologie Sez. Statistica Medica, Brescia, [3]Spedali Civili di Brescia, III Laboratorio Analisi, Brescia, Italy*

Background: Endometrial cancer (EC) is the most common gynaecologic malignancy in the western world. To date, no good marker for EC management is available and CA125, often used in clinical practice, has limited utility. The purpose of this study was to investigate the diagnostic impact of preoperative serum HE4 in EC patients and its relationship with clinicopathologic characteristics.
Material and Methods: The study included 193 EC patients [35 well- (G1), 89 moderately- (G2) and 69 poorly- (G3) differentiated, representatives of all histotypes and stages], 14 patients with endometrial hyperplasia with focal areas of endometrial carcinoma (Hy/EC) and 125 women with normal endometrium (NE) as healthy controls. Pre-operative serum samples were analyzed for HE4 and CA125 levels by a chemiluminescent microparticle immunoassay on automated ARCHITECT instrument (Abbott Diagnostics Division, Chicago, IL).
Results: sHE4 values were significantly higher in EC patients (median = 79.9, mean = 116.0, range 6.5–1348.4), regardless of tumour stage and differentiation grade, compared with NE (median = 39.0, mean = 41.4, range 21.6–84.5) and with Hy/EC (median = 42.6, mean = 47.8, range 24.7–138.9), both $p < 0.001$. Instead, no difference in sHE4 levels was detected between NE and Hy/EC ($p = 0.3475$). The areas under the receiver operating characteristic curves (ROC-AUC) were determined for HE4, CA125 and in combination for discrimination of NE and EC. HE4 had a significantly higher ROC-AUC when compared with CA125 in all EC ($p < 0.0001$), regardless of tumour stage and differentiation grade. ROC-AUC deriving from HE4 and CA125 combination was not significantly increased when compared with HE4 alone ($p = 0.2533$). High sHE4 levels significantly correlate with adnexal involvement, deeper myometrial invasion (M2 vs M0/M1), lymph nodes metastasis, higher stage (>I vs I), lymphovascular invasion, positive peritoneal cytology, higher grade (G2/G3 vs G1), presence of cervical invasion (all $p < 0.01$). No significant difference was detected among different histotypes ($p = 0.638$).
Conclusions: This study highlights that HE4 is secreted at higher levels in serum of EC patients compared with NE controls and it is more sensitive and specific compared to CA125 in distinguishing malignant disease, regardless of tumour stage and grade. sHE4 levels could be associated with a more aggressive tumour phenotype and could be clinically useful in identifying high-risk EC patients for a more aggressive adjuvant therapy.

1460 POSTER

A Novel Lectin Array-based Technology for Non Invasive Cancer Diagnosis via Serum Samples − a Proof of Concept in Gastric Cancer

M. Daniely[1], Y. Reshef[1], Y. Namdar[1], B. Gorelik[2], I. Lieder[2], A. Samokovlisky[3], N. Landes[3], Y. Blumenstein[4], I. Belzer[5]. *[1]Procognia Israel, Glycodiagnostics, Ashdod, [2]Procognia Israel, Bioinformatics, Ashdod, [3]Procognia Israel, Assay Development, Ashdod, [4]Procognia Israel, Production, Ashdod, [5]Procognia Israel, R&D, Ashdod, Israel*

Background: Cancer development is associated with glycosylation alterations of glycoproteins. The aberrant glycoproteins may be detected in malignant cells and secreted or released into blood. We have developed a novel lectin array-based platform that can be utilized to detect unique glycosylation patterns of proteins. Binding of a glycoprotein to the array results in a characteristic fingerprint, highly sensitive to changes in its glycan composition. The results are analyzed by software that uses bioinformatic tools.
Using this technology, we performed a study aimed to identify the presence of gastric cancer via serum samples. Gastric cancer is a common cause of cancer-related death worldwide. It is difficult to diagnose and causes only non-specific symptoms. Therefore, invasive approaches such as endoscopic observation and biopsy are necessary for diagnosis.
Materials and Methods: A cohort of 120 gastric cancer patients and 150 healthy controls were tested using the lectin array (LA) technology. The LA was composed of 30 different lectins, printed in triplicates. 15 μl of serum were depleted from the 14 most abundant proteins, labeled fluorescently and coupled with the LA overnight at 37ºC. LA slides were scanned by a laser scanner and the results were interpreted by the software.
Results: The LA assay was capable to distinguish between samples from gastric cancer patients and controls in a sensitivity and specificity of 80 and 85%, respectively. Several lectins were selected as predictors enabling to differentiate between gastric cancer patients and healthy controls. The LA was equally capable of detecting the disease in samples from early and advanced-stage gastric cancer.
Conclusions: The current study demonstrates the feasibility of using a lectin array-based technology for non-invasive detection of gastric cancer via serum samples, showing high sensitivity and specificity (80 and 85%, respectively). Aberrant glycosylation is well documented to occur in all types of human cancers. The LA provides an easy means to exploit this observation and to translate it into a clinical assay applicable to clinical diagnostics laboratories. The promising results of the current study need to be validated in a large controlled clinical trial. Nevertheless, they imply that this technology can be potentially used as an adjunct diagnostic test for patients suspected for having gastric cancer and provide a proof of concept to its cancer diagnostics potential in general.

1461 POSTER

Hyponatremia (hNa) in Cancer Patients (pts): an Underestimated Problem

L. Benmoussa[1], F. Troalen[2], M. DiPalma[1], T.A. Alibay[1], R. Miron[1], M. Merad-Taoufik[1], S. Antoun[1]. *[1]Institut Gustave Roussy, Day Care, Villejuif, [2]Institut Gustave Roussy, Biology and Medical Pathology, Villejuif, France*

Background: Among biological abnormalities occurring in cancer pts, hNa is often neglected; despite it can bring some severe neurological disorders (such as confusion or coma). Exact prevalence is not known. Etiological investigations are often limited and clinical care not always optimized.
Methods: We conducted a prospective 3-month survey including all the pts consulting at Emergency Service in our institution (a French comprehensive cancer center), whatever the reason of the consultation was and undergoing some blood tests including Natremia (Na). hNa was defined as Na <136 mM/l, severe hNa, as Na <129mM/l: in that case the pt was hospitalized for further investigations and treatment. Anti-diuretic hormone (ADH) level was determined and an hypocorticism was check by performing cortisolaemia dosage and ACTH stimulation test. Biological dehydration was defined as urinary urea/plasma urea > 10.
Results: 1190 pts were included: 32 pts were found with hNa (2.7%), with a mean Na=127±3.6mM/l, (Na ⩽120:3pts, 120 <Na ⩽129:16pts; 130 ⩽Na <136:13pts). Tumour types were predominantly colo-rectal (31%), lung (15%) and gynecologic cancers (12%), 77% pts had metastatic, and 74% progressive disease; 80% receiving chemotherapy, while 22% were treated with targeted therapies. Seventy two % had some biological dehydration. After adequate care (re-hydration for 92% pts) Na improved in all patients: mean Na (mM/l) after 3 days was 132±4.3, after 6 days 134±4.7. Twenty eight % pts had no symptom of clinical or biological dehydration. Hypocorticism could be considered in 21% of pts as basal cortisolaemia was 480±37nM/l and after stimulation 790±217nM/l. All ADH levels were in normal range. One third pts with hNa died within a mean of 32 days (6 to 84 days) after diagnosis of hNa.
Conclusion: hNa in cancer pts is not a rare occurrence. Prevalence can be estimated to 2.7% in ES. In 60% of the cases hNa was considered as severe, leading to pts hospitalization. Dehydration is the main cause of hNa, as it concerned 2/3 pts. Functional hypocorticism could be considered in 21% pts. Of note, hNa seems to be associated with poor prognosis, but this need to be addressed in further study.

1462 POSTER

BRCA 1/2 Mutation Carriage in Healthy Women and Patients With Breast Cancer is Associated With Elevated Serum Thymidine Kinase 1 Activity

B. Nisman[1], L. Kaduri[1], T. Allweis[1], T. Hamburger[1], E. Carmon[2], T. Peretz[1]. *[1]Hadassah Medical Organization, Oncology, Jerusalem, [2]Hadassah Medical Organization, Surgery, Jerusalem, Israel*

Background: The BRCA1 and BRCA2 tumour suppressor genes are involved in the regulation of cellular proliferation and DNA repair. Mutations in these genes confer greater risk of developing breast and ovarian cancer. In this study we explored thymidine kinase 1 (TK1), a pyrimidine metabolic pathway enzyme essential in the salvage DNA synthesis and repair processes.
Patients and Methods: Serum TK1 activity was determined with a high sensitive DiviTum (Biovica) ELISA assay in 5 groups of women, namely, control subjects from healthy blood donors (Group 1, n = 120), healthy carriers of BRCA1/2 mutation (Group 2, n = 67), healthy carriers of BRCA1/2 mutation who underwent preventive bilateral salpingo-oophorectomy (Group 3, n = 33), primary breast cancer (BC) patients non-carriers (Group 4, n = 66) and primary BC patients carriers of BRCA1/2 mutation (Group 5, n = 17).
Results: There was no correlation between serum TK1 activity and age in the control group ($R = 0.07$). The enzyme activity in women from each of the Groups 2−5 was found to be significantly higher than in women

from Group1 (for all $p < 0.001$). Group 2 did not differ from Group 3 ($p = 0.61$). Both BRCA1 ($n = 49$) and BRCA2 ($n = 51$) mutation carriers from the combined Group 2 and 3 ($n = 100$) demonstrated higher serum TK1 activity than healthy women from Group 1 (for all $p < 0.001$). There was no difference in TK1 activity between BRCA1 and BRCA2 mutation carriers ($p = 0.57$). Higher TK1 activity was found in BC patients with BRCA1/2 mutation from Group 5, compared to those without the mutation from Group 4 ($p = 0.002$). The area under the TK1 ROC curve ($\pm$ standard error) in the model considering Group 1 vs. combined Group 2 and 3 was 0.73 ± 0.03. The optimal cut-off value corresponded to 30 Du/L of TK1 activity and supplied a sensitivity of 63.3% and specificity of 77.5% for identifying BRCA1/2 mutation carriers.
Conclusions: BRCA1/2 mutation carriage is significantly associated with elevated serum TK1 activity both in healthy women and in patients with breast cancer.

1463 POSTER

CA19-9 in Combination With Abdominal CT Scan for Diagnosis of Mass-forming Intrahepatic Cholangiocarcinoma

N. Raunroadroong[1], S. Thongprasert[2], N. Lertprasertsuke[3], S. Pojchamarnwiputh[4], W. Na Chiangmai[4], W. Sinsuwan[2], H. Sriplung[5]. *[1]Lampang Cancer Center, Medical Oncology Unit, Lampang, [2]Maharaj Nakorn Chiang Mai Hospital, Department of Medical Oncology, Chiang Mai, [3]Maharaj Nakorn Chiang Mai Hospital, Department of Pathology, Chiang Mai, [4]Maharaj Nakorn Chiang Mai Hospital, Department of Diagnostic Radiology, Chiang Mai, [5]Prince of Songkla University, Epidemiology Unit, Songkla, Thailand*

Background: Cholangiocarcinoma (CCA) is one of the most important cancer in Thailand. The diagnosis of CCA with pathology is widely accepted. Unfortunately, tissue diagnosis of mass-forming intrahepatic cholangiocarcinoma is difficult to perform according to tumour site, risk of procedure and accessibility. The aims of this study are assessing the diagnostic utility of CA19-9 for mass-forming cholangiocarcinoma in combination with CT scan of the liver.
Methods: The medical records of patients with the diagnosis of cholangiocarcinoma (CCA) and hepatocellular carcinoma (HCC) during January 2005 to December 2009 were reviewed. Each case was checked for pathology and CT scan report performed at Maharaj Nakorn Chiang Mai Hospital and excluded each case with either report from other hospitals. Demographic data, clinical manifestation, laboratory results including CA19-9 and CT scan of the liver were carefully examined in order to established the diagnostic utility in mass-forming CCA without pathological diagnosis.
Results: 79 CCA patients and 66 HCC patients were included in CA19-9 cut off levels analysis. 31 CCA patients and 44 HCC patients were included in CT scan characteristics evaluation and scoring according to Chiang Mai CT score for CCA. Chaing Mai CT score for CCA consists of 3 features which are thin/thick rim enhancement at periphery on arterial phase, capsular retraction and dilated bile duct peripheral to tumour giving score 1, 4, and 2 respectively. The specificity of CA19-9 value 500 U/mL in diagnosing CCA was 95.5% with sensitivity 50.6%, PPV 91.8% and likelihood ratio of positive(LR+) 11.24. The CT score greater than 2 demonstrates PPV of more than 90% in diagnosis of CCA. The CA19-9 level of 140 U/mL in combination with CT score 2 demonstrated LR+ as high as 57.09.
Conclusion: CA19-9 level combined with Chiang Mai CT score for CCA are good diagnostic tool for diagnosis of mass-forming cholangiocarcinoma with high specificity, high positive predictive value and high likelihood ratio of positive.

1464 POSTER

Comparison of HER-2 and Hormone Receptor (HR) Status Between Primary Breast Cancer and Corresponding Distant Metastatic Sites With Double Check Assessment

I. Frahm[1], G. Acosta Haab[2], S. Sarancone[3], V. Caceres[4]. *[1]Sanatorio Mater Dei, Pathology, Buenos Aires, [2]Hospital Marie Curie, Pathology, Buenos Aires, [3]Laboratorio Quantum, Pathology, Rosario, Argentina; [4]Productos Roche, Oncology, Buenos Aires, Argentina*

Background: Although the vast majority of breast cancer carcinoma maintains the same biological features at relapse, recent studies suggested that some lesions may have a change in HER2 and HR status during tumour progression. As such, it may be advisable to biopsy metastatic disease for optimal treatment planning.
Aim: To compare HER2 and HR status of metastatic breast cancer with those of the original tumour with simultaneously double check assessment to reduce analytical procedures errors.
Methods: From 2008 to 2010, 118 patients with biopsy proven relapses were identified. HER-2 analysis was performed in both primary and metastasis material. Results were interpreted as hercepTest® guideline's. Discordant cases were evaluated by fluorescence *in situ* hybridization (FISH) too. ER and PR were also screened by IHC analyses.
Results: 118 primary breast cancer tumours and their corresponding distant metastasis were analyzed. Among paired primary/metastatic tumours, we found 13 discordant cases, 8 in ER or PR, 4 in HER 2 showed discordance by IHQ and FISH and1 case in both parameters.
Results are summarized in Table 1.

Table 1: Discordant cases with double check assessment

Primary tumour	ER	PR	HER2	Metastatic site	ER	PR	HER2
1	+	+	0	cervical node	+	−	0
2	+	+	0	Pleura	+	−	0
3	+	+	0	Lung	+	−	0
4	+	+	0	Pleura	−	−	0
5	+	+	0	Ovary	−	+	0
6	+	+	0	peritoneum	−	−	0
7	+	−	0	Bone	+	+	0
8	+	+	0	Skin	−	−	0
9	−	−	1+	Supraclavicular node	−	−	2+
10	+	+	1+	Supraclavicular node	+	+	3+
11	+	+	2+	Liver	+	+	0
12	+	−	0	Liver	−	−	3+
13	+	−	3+	Bone	−	−	0

Conclusions: 13/118 (11%) of relapsed tumours had changes in HER2 or ER or PR status. with double check evaluation The tendency showed a lost in HR and a gain in HER 2 positivity This study suggests that biopsies of relapsed/metastatic breast cancers should be performed, in concordance with largest series recommendations previously published.

Oral Presentations (Mon, 26 Sep, 14:45−16:25)
Radiotherapy

2000 ORAL

Prognostic Value of Metabolic Response Assessed by 18F-FDG PET During Radiotherapy for Cervix and Head and Neck Carcinoma

J. Leseur[1], G. Louvel[1], A. Devillers[2], P. Olivier[3], N. Gillet[4], C. Rodrigues[5], D. Williaume[1], J.D. Ospina Arango[6], E. Garin[2], R. De Crevoisier[1]. *[1]Centre Eugene Marquis, Radiotherapy, Rennes Cedex, France; [2]Centre Eugene Marquis, Nuclear medicine, Rennes Cedex, France; [3]Centre Hospitalier Universitaire, Nuclear medicine, Vandoeuvre les Nancy, France; [4]Centre Hospitalier Régional, Nuclear Medicine, Metz-Nancy, France; [5]Centre Hospitalier Privé, Physics Department, Metz-Thionville, France; [6]Université Rennes 1, Unité INSERM 642, Rennes Cedex, France*

Background: Sequential FDG-PET/CT performed during the course of radiotherapy has been poorly explored and may be an early surrogate of patient outcome. The aim of this study was to analyze metabolic changes during radiotherapy at 40 Gy and its prognostic impact in cervix and head and neck cancer (HNC) patients (pts).
Materials and Methods: This prospective study included 2 populations:
a. HNC: 22 pts. Stages were: II (23%), III (27%) and IV (50%). Primitive tumour sites were: 11 oropharynx, 5 hypopharynx, 1 cavum and 6 larynx. Treatment was: external beam radiation therapy (EBRT) (70 Gy) with concurrent cetuximab.
b. Cervical cancer: 35 pts. FIGO stages were: IB2: 4, IIA: 5, IIB: 11, IIIA: 2, IIIB: 1, IV: 2. Treatment was: EBRT (46 Gy) with concurrent chemotherapy (Cisplatinum), followed by brachytherapy $\pm$ Surgery.

All pts were evaluated by FDG PET: before treatment (PET1), during EBRT at 40 Gy (PET2), and after the end of RT (PET3). Following FDG-PET parameters were analyzed: maximal standardized uptake value (SUVmax) and metabolic tumour volume (MTV). MTV was segmented: by fixed threshold of all voxels >2.5 of SUV for HNC and by a threshold of 40% of SUVmax for cervix cancer. The predictive values of these parameters (as continuous variable or with cut-off values defined by ROC analysis) were searched (Cox model and log rank) for disease free survival (DFS).
Results: Median follow-up was 15 months (3−31) in HNC and 17 months (3−36) in cervix cancer. The 2-year DFS rates were: 53% and 72%, for HNC and cervix cancer, respectively.
– **At PET1**: no metabolic parameter was significant on DFS.
– **At PET2**: SUVmax and MTV were correlated with DFS in univariate analysis ($p < 0.05$) for cervix and HNC. SUVmax >8 for HNC decreased DFS (RR = 3.1, 95% CI: 0.9–10.5, $p = 0.05$). SUVmax >6.3 for cervix cancer (mean value of SUVmax at PET 2) decreased DFS ($p = 0.01$).